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08/842,898	04/17/97	MCCARTHY S	MEI-014CP

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AMY E. MANDRAGOURAS
LAHIVE & COCKFIELD, LLP
28 STATE STREET
BOSTON MA 02109

EXAMINER	
ROMEO, D	
ART UNIT	PAPER NUMBER
1646	//

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Please find ~~below~~ attached a communication from the EXAMINER in charge of this application.

Commissioner of Patents

Office Action Summary	Application No. 08/842,898	Applicant(s) McCarthy
	Examiner David Romeo 6/6/98	Group Art Unit 1646

☒ Responsive to communication(s) filed on *Oct 27, 1997* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-61* is/are pending in the application.

Of the above, claim(s) *23-61* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-22* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-61* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Attachment #1

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-22, drawn to nucleic acids, vectors and host cells, classified in class 435, subclass 69.1.

II. Claims 23-36, drawn to a polypeptide, classified in class 530, subclass 350.

III. Claims 37-49, drawn to a method of modulating CRSP-1 activity with an antagonist, classification dependent upon agonist.

IV. Claims 43-49, drawn to a method of modulating CRSP-1 activity with an agonist, classification dependent upon agonist.

V. Claims 50-55, drawn to a method of treating a disease by administering CRSP-1, classified in class 514, subclass 12.

VI. Claims 56 and 57, drawn to a method of identifying a CRSP-1 therapeutic, classified in class 435, subclass 7.1.

VII. Claims 58 and 59, drawn to a method of measuring CRSP-1, classification dependent upon method.

VIII. Claims 58, 60 and 61, drawn to a hybridization assay, classified in class 435, subclass 6.

2. The inventions are distinct, each from the other because of the following reasons:

The polynucleotides of Invention I are related to the polypeptides of Invention II by virtue of encoding same. The polynucleotide has utility for the recombinant production of the polypeptide in a host cell. Although the polynucleotide and polypeptide are related since the polynucleotide encodes the specifically claimed polypeptide, they are distinct inventions because they are physically and functionally distinct chemical entities, and the polypeptide product can be made by another and materially different process, such as by synthetic polypeptide synthesis or purification from the natural source. Further, the polynucleotide may be used for processes other than the production of the polypeptide, such as a nucleic acid hybridization assay.

The following pairwise combinations of products and methods are independent and distinct, wherein the respective products may neither be produced by, nor used in the respective methods: the product of invention I and the methods of inventions III-VII; the product of invention II and the method of invention VIII.

Inventions I and VIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polynucleotide may be used for processes other than a nucleic acid hybridization assay, such as the production of the encoded polypeptide.

Invention II is related to each of Inventions III-VII as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of invention II can be used in any of the other patently distinct methods of inventions III-VII.

The following pairwise combinations of methods are independent and distinct, wherein each member of a pair performs different functions, using different starting materials and/or process steps: the method of invention III and each of the methods of inventions IV-VIII; the method of invention IV and each of the methods of inventions V-VIII; the method of invention V and each of the methods of inventions VI-VIII; the method of invention VI and each of the methods of inventions VII-VIII; the method of inventions VII and VIII.

3. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, require separate searches and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

4. This application contains claims directed to the following patentably distinct species of the claimed invention: agonist, antagonist, immunoassay, hybridization assay.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 43-49 are generic to an antagonist and an antagonist. Claim 58 is generic to an immunoassay and a hybridization assay.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

5. During a telephone conversation with Attorney Amy Mandragouras on 19 May 1998 a provisional election was made without traverse to prosecute the invention of group I, claims 1-22. Affirmation of this election must be made by applicant in replying to this Office action. Claims 23-61 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Formal Matters

6. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

7. The abstract of the disclosure is objected to because it is not a single paragraph and because it contains legal phraseology, i.e. therefor. Correction is required. See MPEP § 608.01(b).

8. The computer readable form (CRF) of the sequence listing has been entered after the correction of minor errors by the Scientific and Technical Information Center staff. Specifically, the spelling of "organism" was changed for SEQ ID NO:6, an opening "(" was added to SEQ ID NO:1, and the letter "l" was replaced with the number "1" in SEQ ID NOs:3-5.

9. The specification is objected to because at page 1, line 7, there is blank a space where a number indicating a U.S. Patent Application serial number is supposed to be.

Correction is required.

10. The specification is objected to because at page 3, line 5, at page 4, lines 20 and 21, at page 5, lines 10 and 11, and at page 63, line 2 there are blank spaces where either a date and/or an ATCC deposit number are supposed to be. Note that the new address for the ATCC, effective March 23, 1998, is American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209.

11. The application is not fully in compliance the sequence rules, 37 C.F.R. § 1.821-1.825. The specification fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. Specifically, sequences are disclosed in Figure 3 without the appropriate

sequence identifier, i.e. SEQ ID NO:. Applicant may bring the application into compliance by amending either the Figures or the "Brief Description of the Drawings" to recite the appropriate sequence identifier.

Correction is required.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-4 and 6-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding SEQ ID NO:2, and an isolated fragment of a polynucleotide encoding SEQ ID NO:2 wherein said fragment specifically hybridizes under conditions of high stringency to said polynucleotide encoding SEQ ID NO:2, does not reasonably provide enablement for the full scope of the claimed embodiments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a nucleic acid encoding "an CRSP-1 polypeptide". There are no structural or functional limitations to the phrase "CRSP-1 polypeptide". The specification defines a "CRSP-1 polypeptide" as intended to encompass polypeptides comprising SEQ ID NO:2, fragments thereof and homologs thereto and include agonist and antagonist polypeptides (Specification, page 20, full paragraph 2). It is unclear what else "CRSP-1 polypeptide" is intended to encompass. The phrase "an CRSP-1 polypeptide" is reasonably interpreted in light of the specification to encompass any structure that has the activity of Applicants' polypeptide, SEQ ID NO:2. However, the actual functional activity of the instantly disclosed CRSP-1 is not known. Furthermore, there are no working examples of a functional activity of a CRSP-1 polypeptide and it is not possible to predict function from primary amino acid sequence. See Bowie et al. (U) page 1306, column 1, full paragraph 1, wherein it is taught that predicting structure, hence function, from primary amino acid sequence data is extremely complex, and it unlikely the problem will be solved in the near future. The claims encompass nucleic acids comprising nucleotide additions, insertions, substitutions, and deletions of SEQ ID NOs:1 or 3, which may or may not alter the functional activity of the encoded polypeptide. The homology of Applicants SEQ ID NO:2 with the chicken protein (Figure 3) is noted. However, neither is the functional activity of the chicken polypeptide disclosed. The specification does not exemplify any structural homologs of CRSP-1 with the functional activity of CRSP-1 and it is unpredictable whether additional homologs exist and what level of sequence similarity would be shared between these

homologs and the nucleic acids encoding them. Because it is unclear what level of sequence identity would be shared between CRSP-1 and homologs thereof, it is highly unpredictable that as to whether the instantly disclosed CRSP-1 nucleic acid could be used to isolate homologs without undue experimentation. The specification also fails to disclose any additional variants or homologs of the instantly disclosed CRSP-1 nucleic acid and it is unpredictable what functional activity would be characteristic of the encoded polypeptides. There is no guidance in the specification for how the instantly disclosed CRSP-1 nucleic acid can be modified such that a homolog is obtained without affecting the functional activity of the encoded polypeptide. Because the actual functional activity of the polypeptide is not known the skilled artisan would not know how to assay for a polynucleotide encoding a functional protein. The specification fails to provide guidance for how the disclosed nucleic acid molecule can be modified without affecting its functional activity. The skilled artisan is left to perform extensive experiments wherein nucleotide additions, insertions, substitutions, and deletions are made in SEQ ID NO:1 and through trial and error experimentation is left to identify which nucleic acids encode proteins with an undefined functional activity. Such trial and error experimentation is considered to be undue. Furthermore, mere hybridization (claim 20) is not a proxy for producing a functional protein because hybridization is insufficient to provide a coding sequence for a protein. Because the functional activity of the polypeptide is not known it would require undue experimentation for the skilled artisan to determine if a polynucleotide hybridizing to SEQ ID NO:1 encodes a protein that

could be used in accordance with the instant specification. Applicants have not provided guidance for fragments of SEQ ID NO:2 that would retain the functional activity of SEQ ID NO:2. There are no working examples of a fragment of SEQ ID NO:2 other than that which lacks the signal peptide. Further, it is not possible to predict which polynucleotides encoding fragments of SEQ ID NO:2 could be used for the production of antibodies specific for CRSP-1. See Daniel et al. (X) wherein it is taught that approaches to predicting antigenic epitopes based on primary amino acid sequence data were unsuccessful. Furthermore, these same approaches were unsuccessful at predicting known antigenic epitopes. Still further the antigenicity of any particular peptide was dependent upon the carrier (page 540, Abstract). The skilled artisan would have to resort to random trial and error experimentation in order to identify polynucleotides encoding antigenic epitopes of SEQ ID NO:2.

Because Applicant has not enabled the full scope of the claimed polynucleotides, Applicant has also not enabled the full scope of vectors comprising the polynucleotides and host cells comprising the vectors.

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and use the full scope of the claimed invention.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-17 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-16 and 20-22 are indefinite over the recitation of the acronym "CRSP-1" because protein acronyms are arbitrarily assigned and they don't clearly identify a protein in terms of its structure or function. It is suggested that the acronym be spelled out and followed by --(CRSP-1)-- at its first use and in all independent claims.

Claims 4, 8, 9 and 15-17 are indefinite over the recitation of "%homology", "%similarity" and "% identity". The use of terms such as percent homology, percent similarity, and percent identity in connection with a recited amino acid or nucleic acid sequence is vague and indefinite in the absence of a clear description or definition of what the term means. This is because sequence identity between two sequences has no common meaning within the art. See George et al. (V) and Barton (W). The scoring of gaps when comparing one sequence to another introduces uncertainty as to the percent of similarity between two sequences. The term can be defined by the algorithm and parameter values set when using the algorithm used to compare sequences.

Although the specification has a general discussion of percent homology, percent similarity, and percent identity at page 22, full paragraph 1, percent homology, percent similarity, and percent identity vary according to the algorithm and the parameters used. It is not clear which algorithm and which parameters are to be used. The metes and bounds of the claim are not clearly set forth.

Claim 12 is indefinite over the recitation of "functional CRSP-1 polypeptide" because it is not clear what the functional activity of the CRSP-1 polypeptide is. The metes and bounds of the claim are not clearly set forth.

Claims 13 and 14 are indefinite because the phrase "capable of interacting" suggest other necessary but unnamed conditions that are required for interaction and it is not clear what other conditions are required for interaction to occur. Furthermore, it has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. In re Hutchison, 69 USPQ 138. The metes and bounds of the claim are not clearly set forth. It is suggested that the phrase "which interacts" be used instead.

Claim 20 is indefinite over the recitation of "high stringency hybridization conditions" because the specification fails to precisely define "high stringency hybridization conditions". One of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

17. Claims 1, 2, 4, 8 and 12-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Sawada et al. (P, cited by Applicants). Sawada et al. disclose a chicken cDNA encoding a protein of unknown function (Table 2, page 533, GenBank Accession No. D26311). Claims 1 and 2 are drawn to a polynucleotide encoding a polypeptide of no particular structure or function. It is reasonable to conclude that Sawada et al's. cDNA encodes a CRSP-1 polypeptide. The meaning of percent homology, percent similarity, and percent identity are dependent upon the algorithm and parameters used to determine percent homology, percent similarity, and percent identity. It is reasonble to assume that Sawada et al's. cDNA has the recited percent homology, percent similarity, or percent identity with Applicants SEQ ID NO:1 or 3, or that Sawada et al's. cDNA encodes a polypeptide with the recited percent homology, percent similarity, or percent identity, depending upon the algorith and pararmeters used to determine percent homology, percent similarity, and percent identity. Sawada et al's. cDNA comprises a nucleotide sequence of at least about 20 consecutive nucleotides of SEQ ID NO:1 or 3 or the complement thereof (See

Attachment #1, nucleotides 180-202 of Sawada et al.). Sawada et al. discloses a Northern analysis with the cDNA (page 532, column 1, full paragraph 2) and it reasonble to assume that the cDNA was labeled. The meaning of "high stringency hybridization conditions" (claim 20) is not clear and it is reasonable to assume that Sawada et al's. cDNA hybridizes under high stringency hybridization conditions to SEQ ID NO:1 or to the complement thereof, depending upon the meaning of high stringency hybridization conditions.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. Claims 1, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sawada et al. (P, cited by Applicants) as applied to claim 1 above, and further in view of Sambrook et al. (Y). Sawada et al. disclose a polynucleotide encoding an CRSP-1 polypeptide, as discussed above. Sawada et al. do not disclose a vector containing the polynucleotide, or a host cell containing the vector. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to clone Sawada et al's cDNA into a vector, and to

transform or transfect a host cell with the vector, with a reasonable expectation of success, using techniques that are well known in the art. See, for example, Sambrook et al., pages 16.2 and 17.2. One of ordinary skill in the art would be motivated to produce the polypeptide encoded by Sawada et al's cDNA in order to have an abundant supply of a protein of low natural availability. The invention is prima facie obvious over the prior art.

Conclusion

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Romeo whose telephone number is (703) 305-4050. The examiner can normally be reached on Monday through Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957.

Faxed draft or informal communications or official papers filed by fax should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

DSR
June 6, 1998